

CLAIMS

Please amend the following claims:

1. (original) Method for identifying and/or the producing an effector of a calmodulin-dependent peptidyl-prolyl *cis/trans* isomerase (CaMAP) consisting of the following steps:
 - (a) mixing of appropriate amounts of a CaMAP or a CaMAP peptide fragment/derivative with an appropriate amount of calmodulin or of a calmodulin fragment/derivative in an appropriate reaction solution with and without the effector;
 - (b) adding an appropriate amount of an appropriate CaMAP substrate,
 - (c) measuring CaMAP activity; and
 - (d) detecting that the effector is
 - (i) an inhibitor if the CaMAP activity in the reaction solution with the effector is lower than in the reaction solution without the effector; or
 - (ii) an activator if the CaMAP activity in the reaction solution with the effector is higher than in the reaction solution without the effector.
2. (original) Method for screening and/or producing an effector of a CaMAP consisting of the steps of
 - (a) mixing appropriate amounts of a CaMAP or a CaMAP peptide fragment/derivative with an appropriate amount of calmodulin or a calmodulin fragment/derivative in an appropriate reaction solution with and without a sample containing a single or a multitude of compounds which are candidates for an inhibitor or an activator;
 - (b) adding an appropriate amount of an appropriate CaMAP substrate;
 - (c) measuring CaMAP activity; and
 - (d) detecting that the sample

- (i) exhibits inhibitory activity if the CaMAP activity in the reaction solution with the sample is lower than in the reaction solution without the sample; or
 - (ii) exhibits activating activity if the CaMAP activity in the reaction solution with the sample is higher than in the solution without the sample.
- 3. (original) Method according to claim 2, further comprising step
 - (e) fractioning of the sample for which inhibitory or activating activity was detected in step (d) and repeating of steps (a) to (d) until the inhibitor or activator contained in the sample is present in purified form.
- 4. (currently amended) Method according to claim 1, ~~any one of claims 1 to 3~~, wherein the CaMAP is selected from the group consisting of the human CaMAPs FKBP36, FKBP37.7, FKBP44, FKBP51, FKBP52 and Cyp40 and enzymes that are listed in the "Swiss-Prot" database corresponding to the denotation used in this database under FKBP66, FKBP42, AIP_HUMAN, AIP_CERAE, AIP_MOUSE, AIPL1_HUMAN, AILP1_RAT, AILP1_MOUSE, AILP1_RABIT, FKB8_HUMAN, FKB8_MOUSE, FKB5_HUMAN, FKB5_MOUSE, FKB4_HUMAN, FKB4_MOUSE, FKB4_RABIT, FKB7_WHEAT, CYP4_BOVIN and CYP4_HUMAN.
- 5. (currently amended) Method according to claim 1, ~~any one of claims 1 to 4~~, wherein the calmodulin or the calmodulin fragment/derivative is selected from the group consisting of

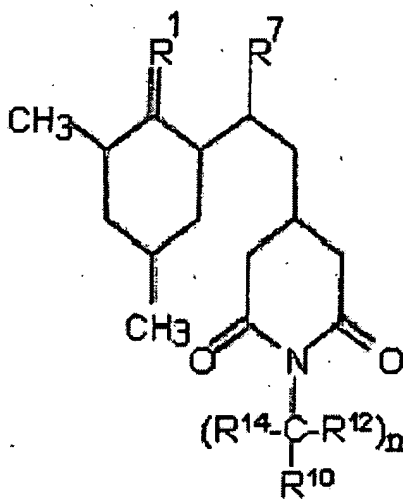
CALM_ACHKL (P15094), CALM_BLAEM (Q9HFX6), CALM_CANAL (P23286),
CALM_CAPAN (P93087), CALM_CHLRE (P04352), CALM_DICDI (P02599),
CALM_DROME (P07181), CALM_ELEEL (P02594), CALM_EMENI (P19533),
CALM_EUGGR (P11118), CALM_FAGSY (Q39752), CALM_HELAN (P93171),
CALM_HORVU (P13565), CALM_HUMAN (P02593), CALM_KLULA (O60041),
CALM_LYCES (P27161), CALM_LYTPI (P05935), CALM_MAGGR (Q9UWF0),
CALM_MAIZE (P41040), CALM_MALDO (P48976), CALM_MEDSA
(P17928), CALM_METSE (P02596), CALM_NEUCR (Q02052), CALM_ORYSA
(P29612), CALM_PARTB (P07463), CALM_PATSP (P02595), CALM_PHYIN
(P27165), CALM_PLAFA (P24044), CALM_PLECO (P11120), CALM_PNECA
(P41041), CALM_PYUSP (P11121), CALM_SCHPO (P05933), CALM_SOLTU

(P13868), CALM_SPIOL (P04353), CALM_STUA (P21251), CALM_STRPU
(P05934), CALM_STYLE (P27166), CALM_TETPY (P02598), CALM_TETTH
(Q05055), CALM_TRYBB (P04465), CALM_TRYCR (P18061), CALM_WHEAT
(P04464), CALM_YEAST (P06787), Q9UWF0, Q02052, P19533, AAL89686,

Q7M510, Q96TN0, P27165, AAG01043, P02593, Q7T3T2, Q40302, O02367, Q95NR9, Q9UB37, AAH54805 AAH54973, AAL02363, AAH59427, AAH59500, AAH54600, AAH53150, AAH50926, AAH45298, AAH44434, AAP88918, AAP35501, AAP35464, BAC56543, AAC83174, AAD55398, AAC63306, AAD45181, AAH21347, BAC40168, BAB28631, BAB28319, BAB28116, BAB23462, AAH58485, AAH51444, AAH47523, P07181, Q7QGY7, Q8STF0, AAO25039, AAM50750, AAK61380, BAB89360, O94739, P02594, Q9D6G4, O16305, Q96HK3, P11120, O96102, P21251, Q9U6D3, Q8X187, Q93410, AAR10240, P11121, Q9XZP2, Q42478, AAQ01510, P17928, P93171, O97341, O96081, AAD10244, AAM81203, AAA34238, AAA34014, AAA34013, P02596, P93087, Q43699, CAD20351, BAB61916, BAB61915, AAF65511, P02595, P59220, P27162, Q93VL8, Q39447, Q94801, AAQ63462, AAQ63461, AAM81202, BAB61918, BAB61917, BAB61914, BAB61913, BAB61912, BAB61911, BAB61910, BAB61909, AAG27432, AAG11418.

6. (currently amended) Method according to claim 1, ~~any one of claims 1 to 5~~, wherein the appropriate reaction solution contains bivalent ions selected from the group consisting of Zn^{2+} , Cu^{2+} , Co^{2+} , Ni^{2+} , Mn^{2+} , Ca^{2+} and/or Mg^{2+} at a concentration of 0,1 to 20 mM.
7. (currently amended) Method according to claim 1, ~~any one of claims 1 to 6~~, wherein the appropriate reaction solution has a pH of between pH 5 and pH 10.
8. (original) Method for identifying and/or producing an effector of a CaMAP consisting of the steps
 - (a) mixing appropriate amounts of a constitutively active CaMAP in an appropriate reaction solution with and without effector;
 - (b) adding an appropriate amount of an appropriate CaMAP substrate;
 - (c) measuring CaMAP activity; and
 - (d) detecting that the effector is
 - (i) an inhibitor if the CaMAP activity in the reaction solution with the effector is lower than in the reaction solution without the effector; or

- (ii) an activator if the CaMAP activity in the reaction solution with the effector is higher than in the reaction solution without the effector.
9. (currently amended) Method according to claim 1, ~~any one of claims 1 to 8~~, wherein steps (a) and (b) are interchanged.
10. (currently amended) Method according to claim 1, ~~any one of claims 1 to 9~~, wherein the detection is carried out by spectroscopic or radioactive methods.
11. (currently amended) Method according to claim 1, ~~any one of claims 1 to 10~~, wherein the method is a high-throughput method.
12. (currently amended) Method according to claim 1, ~~any one of claims 1 to 11~~, further comprising step
- (f) formulating the identified and/or produced effector with a pharmaceutically acceptable carrier or solvent.
13. (currently amended) Compound identified according to the method of claim 1, ~~any one of methods 1 to 11~~, wherein the effector is a cycloheximide derivative having the general formula (1):



in which n is an integer from 1 to 20; R^{12} independently is a hydrogen atom, an alkyl residue or an aryl residue,

R^1 is selected from an oxygen atom, a sulfur atom, or the groups NR^2 , NOR^2 and $N-NR^2R^3$, wherein

- (a) R^2 and R^3 , independently from each other, are a hydrogen atom, aryl or alkyl, respectively, which can optionally be interrupted by O, S, NH, NR^5 , aryl, heteroaryl, cycloalkyl, heterocycloalkyl or can optionally be substituted by R^6 , or
- (b) R^2 and R^3 , together, are C_1 - C_6 -alkylene, which can optionally be interrupted by O, S, NH, NR^5 , aryl, heteroaryl, cycloalkyl or heterocycloalkyl or can optionally be substituted by R^6 , wherein R^5 is an alkyl residue or an aryl residue, R^6 stands for a hydrogen atom, alkyl, aryl, OR^5 , $C(O)OR^5$, CN, F or Cl, wherein R^5 is defined as above,

R^7 is a $-OH$, $-OR^9$, $-OC(O)R^9$, $-OC(S)R^9$, $-OC(O)NHR^9$ or $-OC(S)NHR^9$ residue, wherein

R^9 is an alkyl residue which can optionally be interrupted by O, S, NH, NR^5 , aryl, heteroaryl, cycloalkyl or heterocycloalkyl or can optionally be substituted by R^6 as defined above, or alternatively

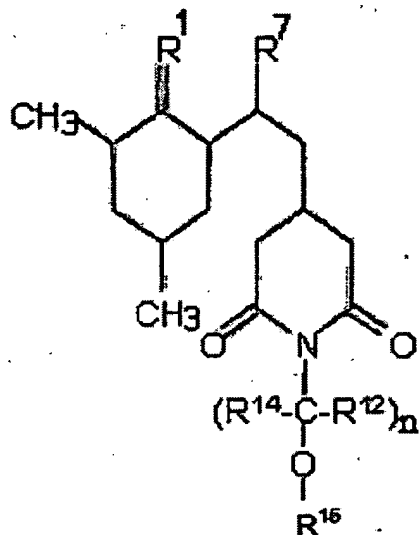
R^9 is an aryl residue which can optionally be interrupted by O, S, NH or NR^5 or can optionally be substituted by R^6 as defined above,

R^{10} is a $-NHR^2$, $-NR^2R^3$, $-C(O)OR^2$, $-C(S)OR^2$, $-C(O)NR^2R^3$, $-CN$, $-NR^2C(O)NR^2R^3$, $-OC(O)NR^2R^3$, $-NR^2C(S)NR^2R^3$, $-OC(S)NR^2R^3$, or OR^2 , $C(O)NHR^{11}$ residue, wherein R^2 and R^3 are defined as above,

R^{11} stands for an amino acid residue or an oligopeptide residue and

R^{14} is an alkyl residue or an aryl residue.

14. (currently amended) Compound identified according to the method of claim 1, ~~any one of methods 1 to 11~~, wherein the effector is a cyclohexamide derivative having the general formula (1) in which n is an integer of 1 to 20 and exhibiting an ether group between R^{15} and the complete molecule as illustrated in formula (2) below,



R^1 is selected from an oxygen atom, a sulfur atom, or the groups NR^2 , NOR^2 and $N-NR^2R^3$, wherein

- (a) R^2 and R^3 , independently from each other, are a hydrogen atom, aryl or alkyl, respectively, which can optionally be interrupted by O, S, NH, NR^5 , aryl, heteroaryl, cycloalkyl, heterocycloalkyl or can optionally be substituted by R^6 , or
- (b) R^2 and R^3 , together, are C_1 - C_6 -alkylene, which is optionally interrupted by O, S, NH, NR^5 , aryl, heteroaryl, cycloalkyl or heterocycloalkyl or can optionally be substituted by R^6 , wherein
 R^5 is an alkyl residue or an aryl residue,
 R^6 stands for a hydrogen atom, alkyl, aryl, OR^5 , $C(O)OR^5$, CN, F or Cl,
wherein R^5 is defined as above,

R^7 is a $-OH$, $-OR^9$, $-OC(O)R^9$, $-OC(S)R^9$, $-OC(O)NHR^9$ or $-OC(S)NHR^9$ residue, wherein

R^9 is an alkyl residue which can optionally be interrupted by O, S, NH, NR^5 , aryl, heteroaryl, cycloalkyl or heterocycloalkyl or can optionally be substituted by R^6 as defined above, or alternatively

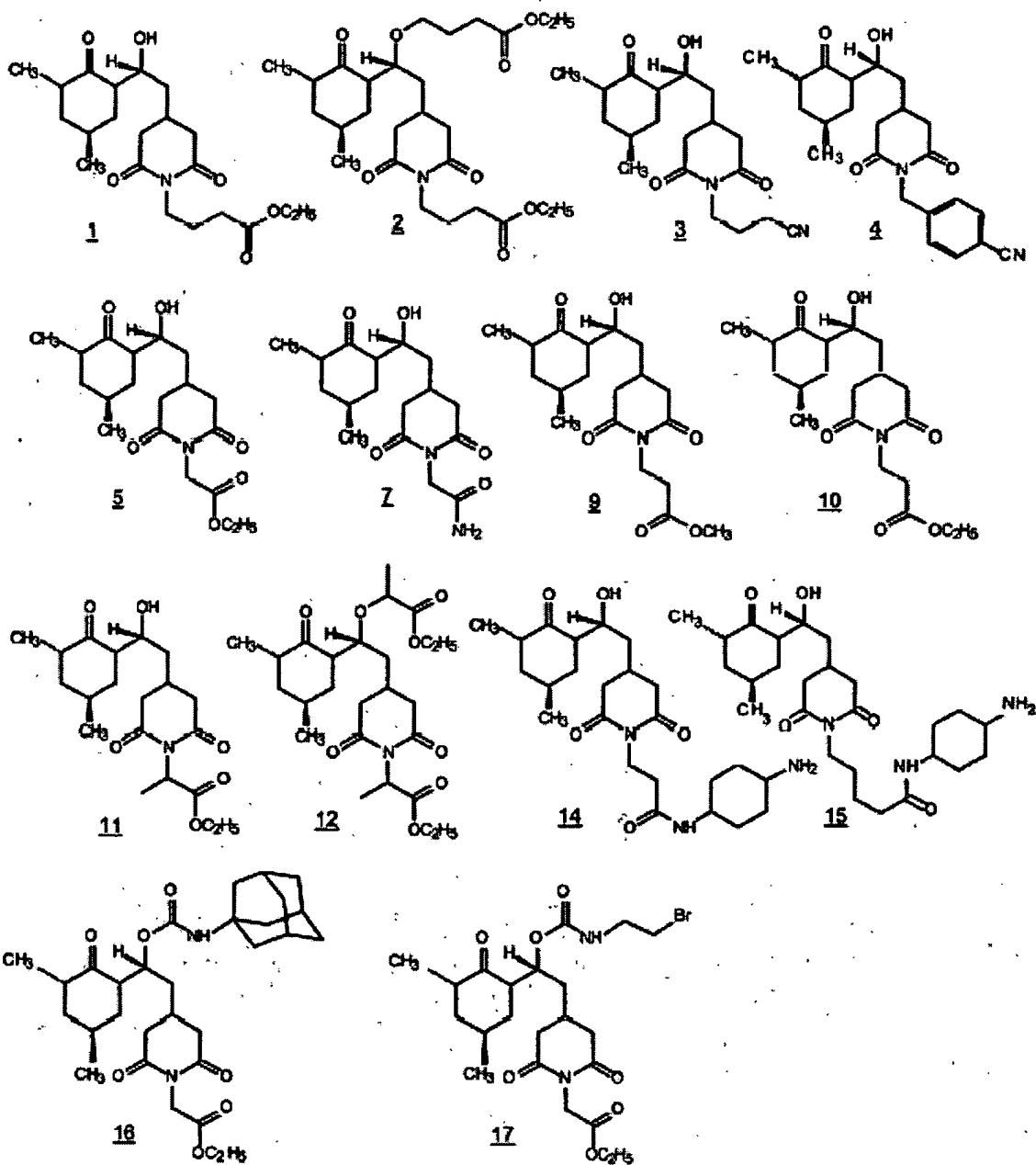
R^9 is an aryl residue which can optionally be interrupted by O, S, NH or NR^5 or can optionally be substituted by R^6 as defined above,

R^{11} stands for an amino acid residue or an oligopeptide residue,

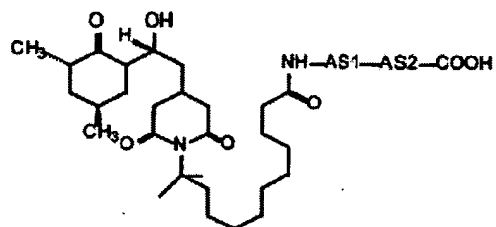
R^{14} is a hydrogen atom, and

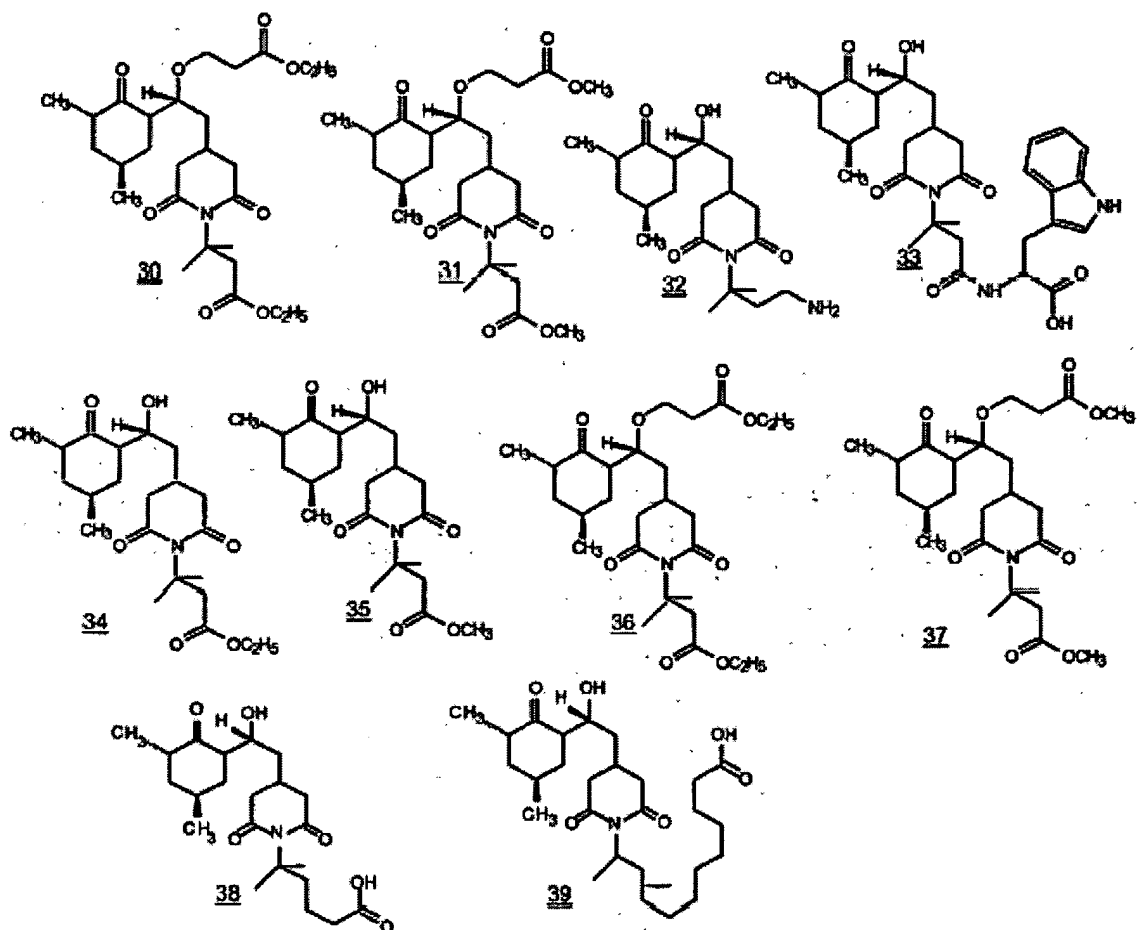
R^{15} is a hydrogen atom, an alkyl or an aryl residue.

15. (currently amended) Compound according to claim 13 ~~or 14~~ having the above-identified formula (1) for which the following applies:
- (a) $n = 1, 2, 3$; $R^1 = O$; $R^7 = OH$, $O(CHR^{12})_nR^{10}$, $OC(O)CH_3$; $R^{10} = C(O)OCH_3$, $C(O)OC_2H_5$, CN , $C(O)NH_2$,
 - (b) $n = 3-10$; $R^1 = O$; $R^7 = OH$; $R^{10} = C(O)NHR^{11}$, $R^{11} = \text{amino acid residue}$, oligopeptide residue,
 - (c) $n = 1, 2, 3$; $R^1 = O$; $R^7 = OH$, $O(CHR^{12})_nR^{10}$; $R^{10} = C(O)OCH_3$, $C(O)OC_2H_5$, CN , $C(O)NH_2$,
 - (d) $n = 1, 2, 3$; $R^1 = NOH$, $N-NHPh$, $N-NHCH_3$, $N\text{-alkyl}$, $N\text{-benzyl}$; $R^7 = OH$, $O(CHR^{12})_nR^{10}$; $R^{10} = C(O)OCH_3$, $C(O)OC_2H_5$, CN , $C(O)NH_2$,
 - (e) $n = 1, 2, 3$; $R^1 = O$; $R^7 = OH$, $O(CHR^{12})_nR^{10}$, $OC(O)NH\text{-alkyl}$, $OC(O)NH\text{-cycloalkyl}$, $OC(O)NH\text{-aryl}$; $R^{10} = C(O)OCH_3$, $C(O)OC_2H_5$, CN , $C(O)NH_2$.
16. (currently amended) Compound according to claim 13 selected from one of the following compounds ~~claims 13 to 15 with the above identified formula:~~



compound	amino acid residue AS1	amino acid residue AS2
<u>18</u>	alanine	alanine
<u>19</u>	valine	alanine
<u>20</u>	tryptophan	alanine
<u>21</u>	isoleucine	alanine
<u>22</u>	methionine	alanine
<u>23</u>	glycine	alanine
<u>24</u>	alanine	valine
<u>25</u>	valine	valine
<u>26</u>	tryptophan	valine
<u>27</u>	isoleucine	valine
<u>28</u>	methionine	valine
<u>29</u>	glycine	valine





17. (currently amended) The effector identified and/or produced by the process of claim 1, Effector according to any one of claims 1 to 16, optionally with a pharmaceutically acceptable carrier or solvent.
18. (currently amended) Use of an effector according to any one of claims 1 to 16 for the preparation of a medicament A method for the treatment of tumour diseases comprising administering an effector of claim 1 to a patient in need thereof in an amount effective to treat a tumour disease.
19. (currently amended) Use of an effector according to any one of claims 1 to 16 for the preparation of a medicament A method for the inhibition or attenuation of transplant rejection or for the treatment of neurodegenerative diseases comprising administering an effector of claim 1 to a patient in need thereof in an amount

effective to inhibit or attenuate transplant rejection or to treat neurodegenerative disease.

20. (currently amended) A kit ~~Kit~~, comprising CaMAP or a peptide fragment/derivative as described in claim 1 ~~or~~ 4 and calmodulin or a calmodulin fragment/derivative as described in claim 1 ~~or~~ 5, one or more buffer solutions and/or one or more substrates.